Avian influenza: Ferret H7N9 flu model questioned

Marc Lipsitch, Harvard School of Public Health, Boston, Massachusetts, USA, mlipsitc@hsph.harvard.edu

David Fisman, University of Toronto, Ontario, Canada.

Joshua B. Plotkin, University of Pennsylvania, Philadelphia, Pennsylvania, USA.

Lone Simonsen, George Washington University School of Public Health and Health Services, Washington DC, USA.

Correspondence published in *Nature* **501**,33 (05 September 2013)
doi:10.1038/501033e

Published online 04 September 2013 with the title (supplied by the journal)
"Avian Influenza: Ferret H7N9 Flu Model Questioned"

We question the relevance to human pandemics of studies designed to investigate transmissibility of the avian influenza A(H7N9) virus between ferrets (M. Richard *et al*. *Nature* http://doi.org/njc 2013; see also R. A. M. Fouchier *et al*. *Nature* **500**, 150–151; 2013).

Earlier studies have demonstrated ferret transmission of wild-type A(H7N9) virus (H. Zhu *et al*.*Science* **341**, 183–186; 2013; and Q. Zhang *et al*. *Science* **341**, 410–414; 2013). However, the results are in striking contrast with the evidence that human-to-human transmission is extremely infrequent.

The discrepancy between ferret and human transmission in some strains undermines the purported value of 'gain-of-function' (GOF) experiments, which track genetically modified variants of A(H7N9). Yet these studies and a proposal to do GOF experiments (R. A. M. Fouchier *et al*.*Nature* **500**, 150–151; 2013) have been published without seriously questioning the relevance of the ferret model.

A naturally occurring virus could differ subtly from any produced experimentally. In that case, human transmissibility, antigenicity and drug resistance would need to be assessed by studies of the actual strain of virus, and data from GOF experiments could in fact be misleading.

The irony of GOF studies is that these results are likely to be useful for public health only if the pandemic arises from a lab accident, as many fear could happen if this work proliferates.